Cancer Care Ontario
Action Cancer Ontario

The Mystery of Ontario's Unusually High Pancreatic Cancer Survival

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Outline

- The mystery & the clues
- The suspect & the evidence
- A possible solution
- Conclusions and further sleuthing

The mystery

- C-SPAN (Cancer survival & prevalence analytic network) calculated survival for major cancers using the CCR:
  - Ages 15-44, 45-54, 55-65, 65-74, 75-99
  - Diagnosis years 1992-94, 1995-97, 1998-2000, 2001-2003*, 2004-2007*
  - Province, Sex (where possible)
  - 1, 3, 5, & 10 year relative survival

The mystery

- For most estimates, Ontario's survival were similar to those from other provinces
- For pancreatic cancer, Ontario's survival was unusually high
  - 2004-07, 5-year age-standardized period relative survival estimate: Ontario, 10.2; other provinces, 3.4 to 5.9

The clues

- Age group, diagnosis period and time since diagnosis were examined to determine, if possible, how Ontario's survival differs from the other provinces.
- Ontario's survival was different for:
  - 15-44, 1-year, all periods
  - 65-74 & 75-99, 3- & 5-year, all periods
  - 2001-3 & 2004-7 periods, 3-year, all ages

Data quality suspect #1

- Incorrect inclusion/exclusion of cases
  - If residence is missing, include
  - ON's conservative multiple primary rules
  - Too many surgery without pathology cases; maybe not really cancer?
  - Autopsy only and death certificate only cases routinely excluded from survival analyses

Data quality suspect #2

- Bias in determination of diagnosis date
  - Hall et al, 2006, compared head and neck cases from the OCR to a clinical series and found that diagnosis dates in the OCR were significantly earlier
  - This can also occur when two primaries are resolved as one.

Data quality suspect #3

- Bias in determination of vital status
  - National death clearance does not include Quebec
  - Can not use the provincial health insurance file to censor those who emigrate from the province

These issues overlap!

- Example: Death certificate only
  - Incident case may have been diagnosed elsewhere
  - No match to case due to linkage failure
  - Date of diagnosis unknown, but survival tends to be short
  - Cause of death may be inaccurate (Hall et al, cause of death had 31% error rate)

Follow the Evidence!

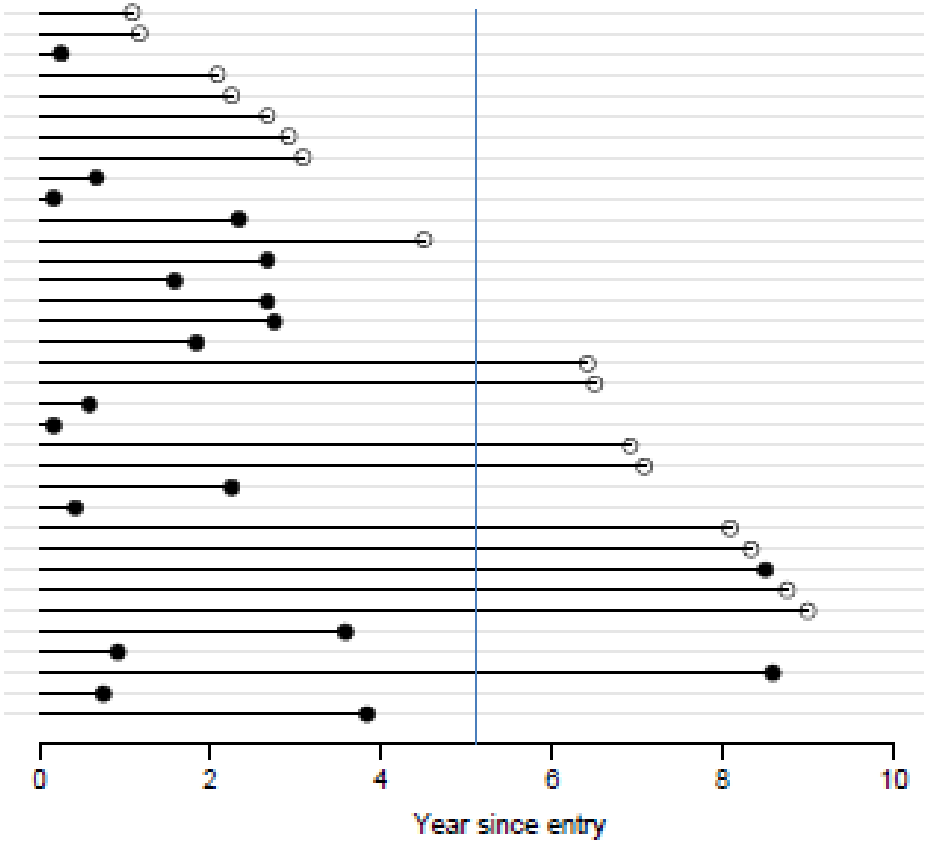
The culprit: lost to follow-up

- Ontario uses only passive registration methods
  - Relies on linkages to mortality data or reports from treatment clinics and hospitals for vital status and date of death
- Usual assumption: cases lost to follow-up are alive at the end of the study

Ontario pancreas data

- 12,379 cases diagnosed 1992-2003
- Followed to December 31, 2008
- Excludes
  - 700 DCO cases (5.3%)
  - 7 Autopsy only cases
  - 26 cases with missing residence

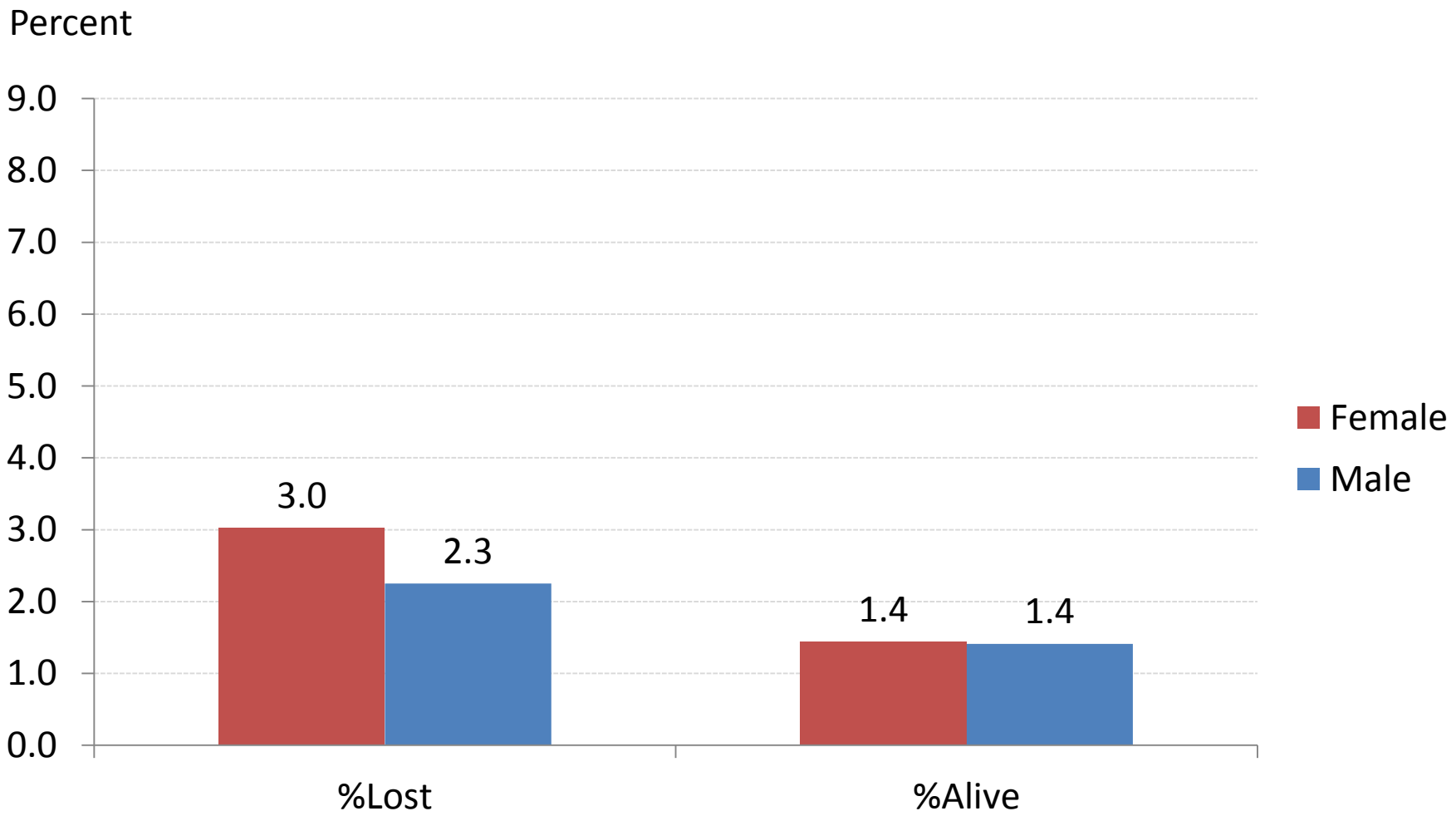
Sample survival data



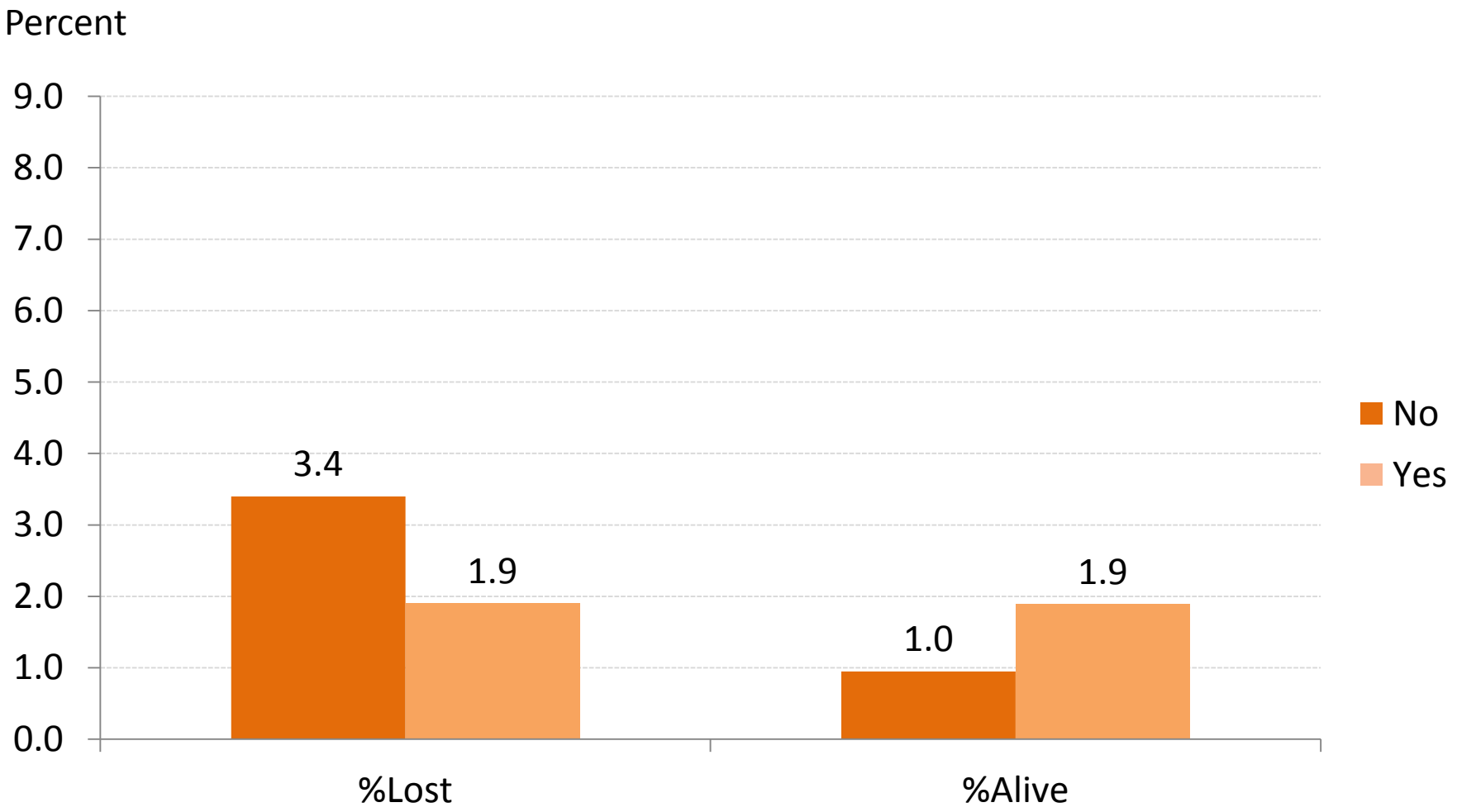
%Lost=8/35
=22.9%
%Alive=10/27
=37.0%

- Finnish colon cases (Dickman & Lambert)

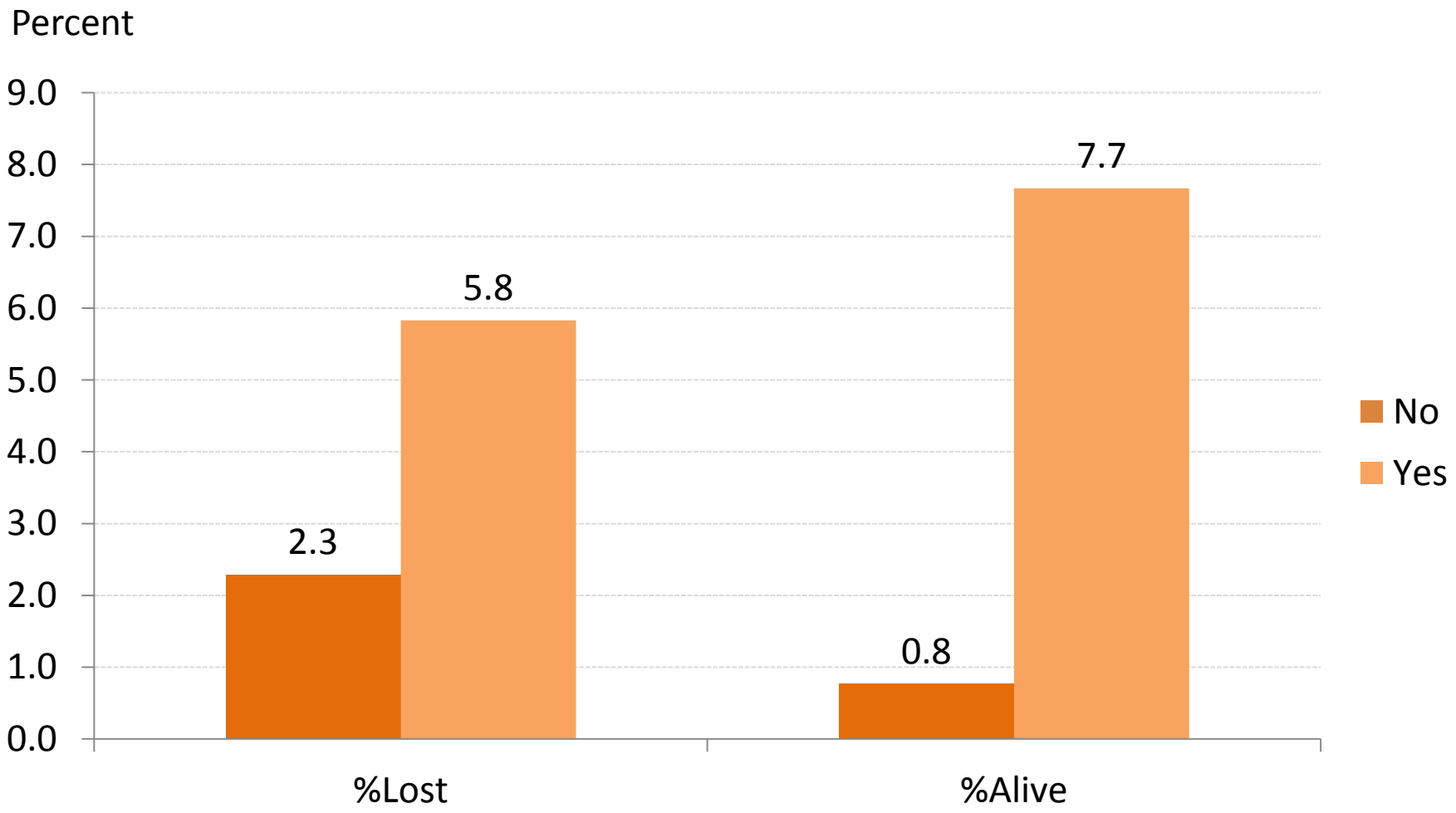
Follow-up & survival: sex



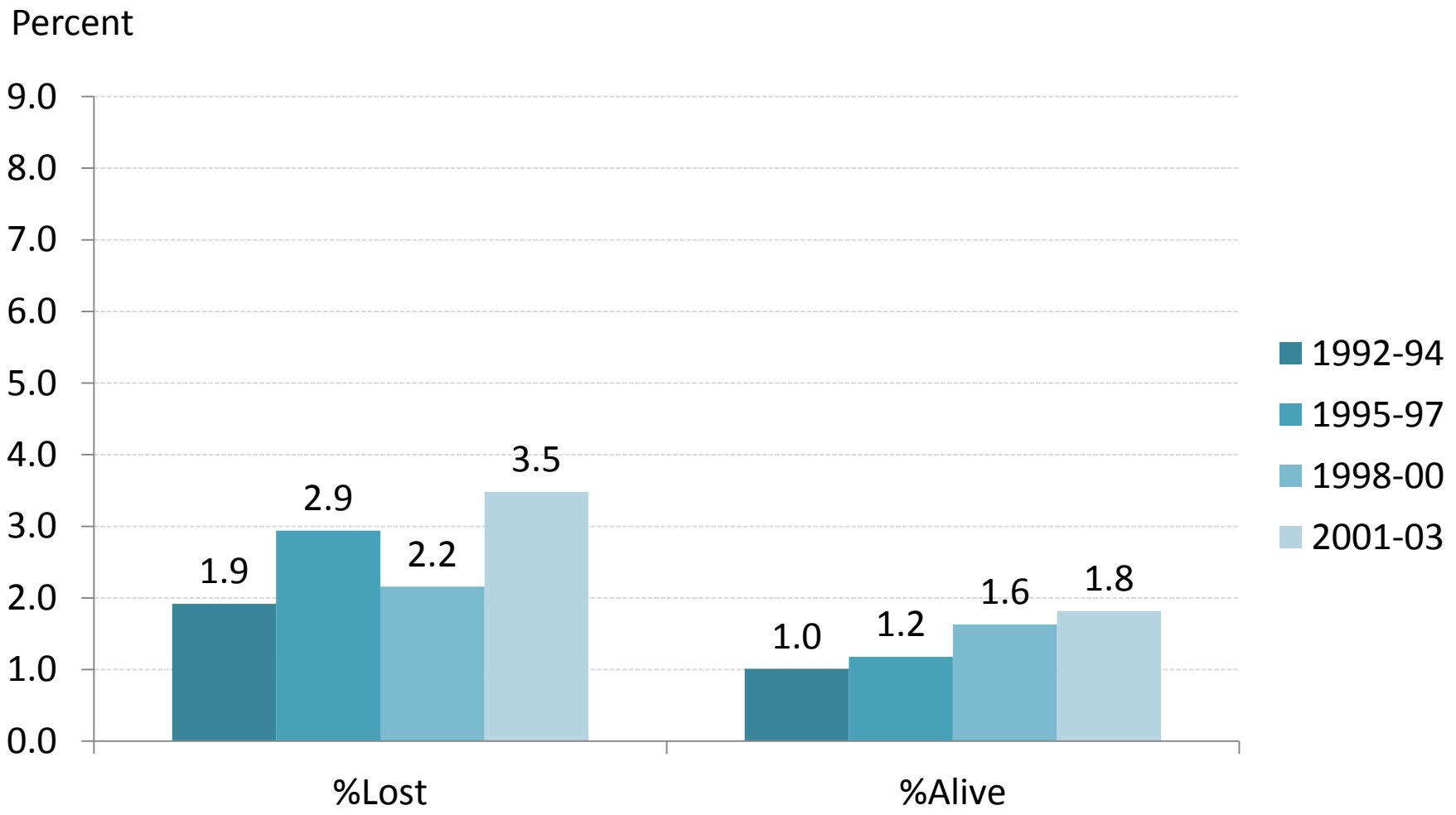
Microscopic confirmation



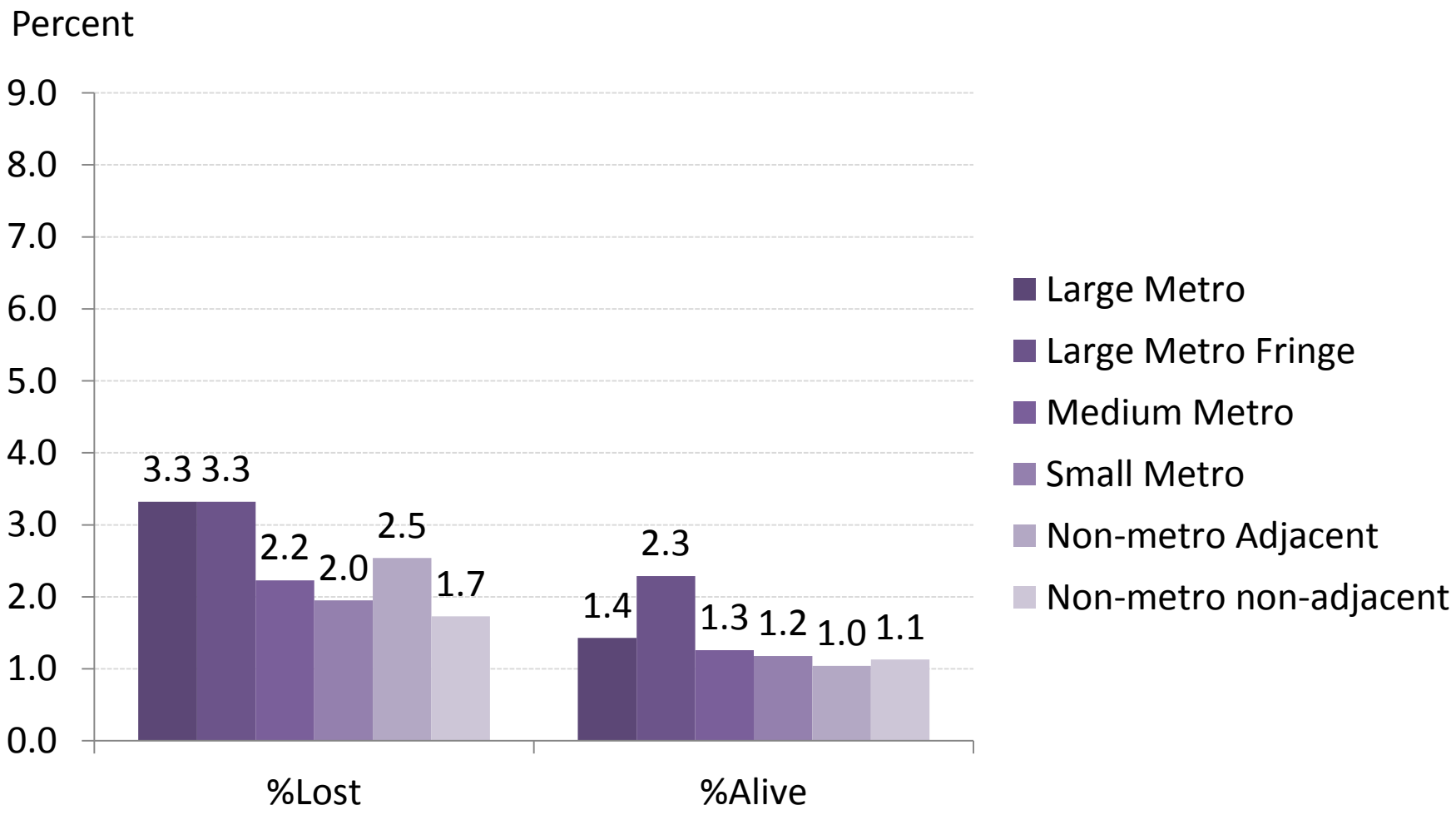
Surgery



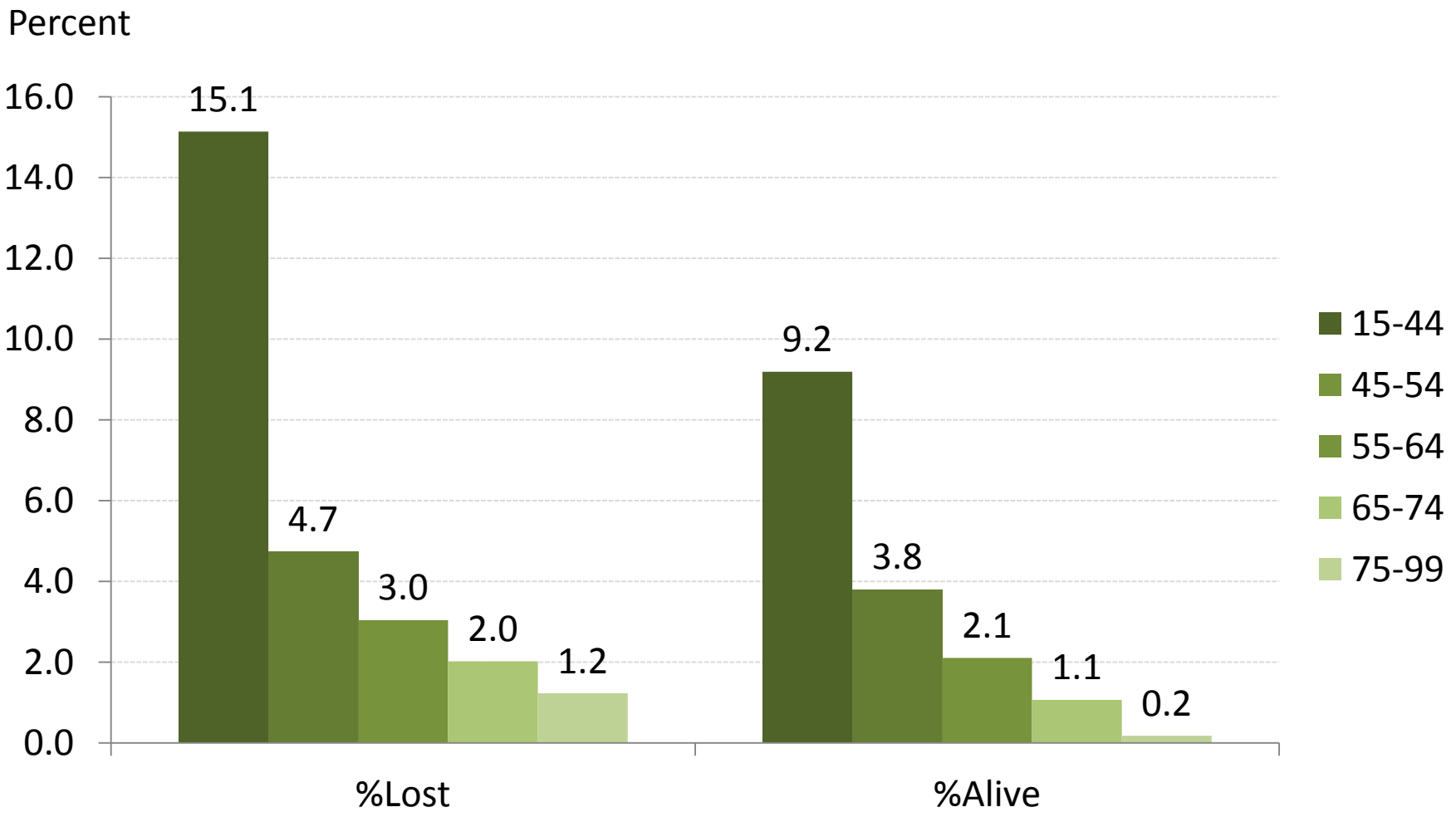
Diagnosis period



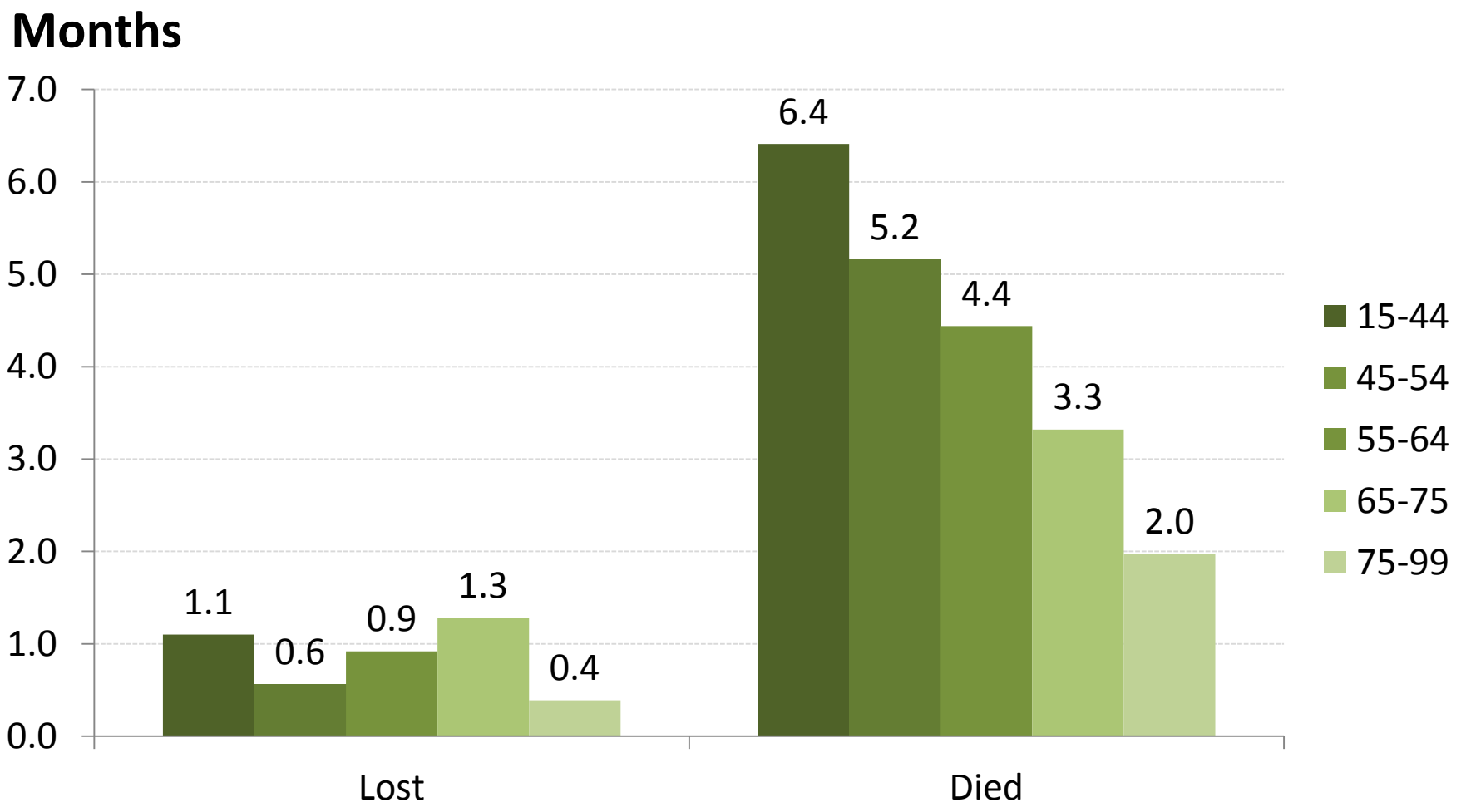
Beale code


Percent
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
3.3
3.3
2.2
2.0
2.5
1.7
1.4
2.3
1.3
1.2
1.0
1.1
%Lost
%Alive
Large Metro
Large Metro Fringe
Medium Metro
Small Metro
Non-metro Adjacent
Non-metro non-adjacent

Age group


Percent
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
15.1
4.7
3.0
2.0
1.2
9.2
3.8
2.1
1.1
0.2
%Lost
%Alive
15-44
45-54
55-64
65-74
75-99

Median observed time



Paper #1

- Brenner & Hakulinen (2009)
- Finnish Cancer Registry, 20 common cancers, dx 1985-9, follow-up 2004
- Under-ascertainment of deaths:
  - Imperfect death linkage, 0.1-5%
  - Unregistered emigration, 0.05-2%

Paper #1 Results

- “Even modest levels of under-registration of deaths may lead to severe overestimation of long-term survival estimates”
- Worse for
  - Relative survival
  - Older ages
  - Unrecorded emigration

Paper #2

- Johnson, Weir, Yin & Niu (2010)
- SEER data, SEER site recode, dx 1995-2000, follow-up 2005
- Characteristics of synthetic datasets:
  - Incomplete death ascertainment: 2%-10%
  - Follow-up of live patients: none, or incomplete (5%-30%)

Paper #2 Results

- When death ascertainment is *complete*
  - Minor differences with no follow-up
  - As loss increases, survival estimates decrease
  - Impact greatest for cancers with very high or very low case fatality rates

Paper #2 Results

- When death ascertainment is *incomplete*
  - Missing even a small proportion of deaths resulted in high survival
  - Impact of missing deaths most evident for cancers with high fatality rates

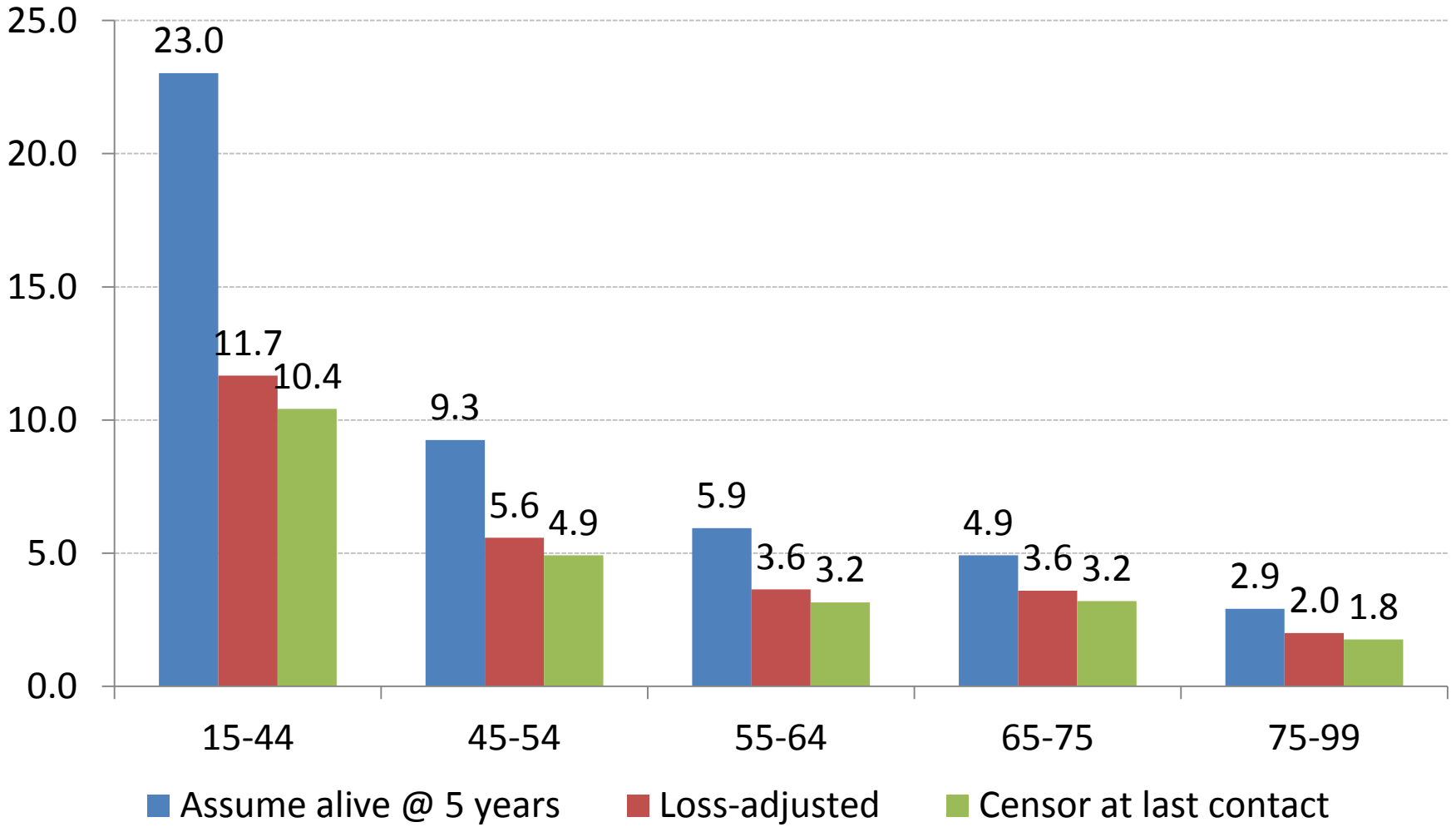
What's up with ON?

- Large, growing immigrant population
  - Return to homeland after diagnosis?
- No alternate sources for residence/vital status verification
- Incomplete national death clearance

Loss-adjusted survival

- “Cancer survival in Africa, Asia, the Caribbean and Central America”, IARC 2011. (Chapter 2, Ganesh et al)
- Estimated by assuming that survival of patients lost to follow-up is the same as that for patients with known follow-up and similar prognostic factors.

Observed 5-year survival



Conclusions

- The assumption that cases lost to follow-up are alive at the cut-off date appears to be responsible for the bias in Ontario's high pancreatic cancer survival
- The impact of emigration may be greater than expected elsewhere
- Additional linkages should be considered to improve follow-up

Next steps

- Loss correction:
  - Adjust for multiple prognostic factors
  - Explore relative survival and period method
  - Analyze other cancers, especially lung, liver and melanoma
- Further explore the DCOs

References

- Hall S et al. “Using cancer registry data for survival studies: the example of the Ontario Cancer Registry”, J Clin Epi 59 (2006): 67-76.
- Brenner H and Hakulinen T. “Implications of incomplete registration of deaths on long-term survival estimates from population-based cancer registries.” Int J Cancer 125.2 (2009): 432-37.
- Johnson CJ, Weir HK, Hin D, Niu X. “The impact of patient follow-up of population-based survival rates”, J Registry Management 37.3 (2010): 86-103.
- Sankaranarayanan R, Swaminathan R, Lucas E. Cancer survival in Africa, Asia, the Caribbean and Central America (SurvCan). IARC Scientific Publications volume 162, ISBN 978-92-832-2162-3, Lyon, International Agency for Research on Cancer (2011).